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SOME REMARKS ON STOVAINE

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I fully realized when you did me the honour of electing me your president for the ensuing year that I should have to address you on some subject of general interest and more particularly of direct interest to us as anæsthetists.

This is by no means an easy matter because there appears to be great doubt about the functions and usefulness of the specialist anæsthetists, not only in the lay mind, but in the minds of some surgeons.

Many in each group appear to regard us as almost unavoidable evils mitigated by varying degrees of necessity or possibly usefulness.

In my conception we should avail ourselves of *all* the known means at our disposal to help the patient, the surgeon, and the advancement of our specialty. This we can never do unless we take the lead in those subsidiary branches of our art, namely, Regional and Spinal Analgesia and show that we are not content to be regarded solely as haphazard purveyors of unconsciousness.

My chief reason for selecting "Stovaine Analgesia" as the subject of my remarks, is that, in conversation with surgeons and anæsthetists of proved ability, I find the most divergent opinions not only of its usefulness, but even of the justification of its use.

Secondly, my experience in spinal analgesia is almost entirely confined to that produced by stovaine. Novocaine

I have used on a few occasions but not sufficiently often to enable me to express an opinion.

Before indulging in an analysis of some cases in which stovaine was used either alone or in conjunction with a light inhalation anæsthesia, I fear that I must call your attention, however needlessly, to some general points in spinal analgesia. I will endeavour to be brief and confine myself only to those points of direct interest to the anæsthetist, or which might prejudice the result.

I. Anatomical Considerations and Physiological.

The general anatomy of the spinal column and cord I take to be known to all of us, but we should particularly remember that the cord extends in the adult to the lower border of the first lumbar vertebra and in children to the third lumbar vertebra. Bending the spine forward raises a little the level to which the cord descends. The cord and cauda equina are invested by their pia, arachnoid and dura mater as far down as the middle of the sacral canal or lower border of the second sacral vertebra.

Imbrication of spinal processes varies greatly not only in the individual but at different regions of the vertebral column, being greatest at lumbar region, while from dorsal upwards very nearly straight. This is of importance when making the puncture. Average depth of theca from skin, 7-10 cm. in adult and 2½ cm. children.

It is thus possible to introduce drugs into the subarachnoid and cerebro-spinal fluid below the termination of the spinal cord. A septum pia mater—ligamentum denticulatum—has been described as separating the subarachnoid space into anterior and posterior divisions above the level of the cord. This possibly explains some of the cases in which complete analgesia is obtained (P.N. Rts) but in which motor activity persists in varying degrees (A.N. Rts). The origin of the cerebro-spinal fluid is from the choroid plexuses. Average amount is 120-130 c.cs. and Sp. Gr. 1004-1007. It is in constant motion, being driven out of the cranium with each arterial beat into the spinal subarachnoid. Coughing, straining and forcible respiration tend to drive the fluid from lumbar cul-de-sac upwards to cervical region. The pressure

varies directly with that of the cerebral circulation and Dandy[1] estimates that the cerebro-spinal fluid is completely replaced about five times per diem. The cerebro-spinal fluid bathes the cord and spinal nerve roots and communicates with that in the fourth ventricle through the foramen of Magendie and it also bathes the following cranial nerve roots—oculomotor, trochlear, abducent and optic.

II. Chemistry.

Stovaine hydrochloride is the salt used to produce spinal analgesia and I do not wish to reiterate to you what its specific chemical characters are, but will content myself by saying —it is soluble in $1\frac{1}{4}$ pts. water and in alcohol 4 pts. It is precipitated by alkalies and small traces of alkali render its analgesic properties much less efficient. It is, in crystals and in solution, stable and capable of sterilisation at 115°C. without decomposition. It is reckoned to be as powerful a local analgesic as cocaine but one-third of its toxicity. In concentrations of more than .75—1 per cent. it has been reported to cause gangrene of the tissues. The maximum safe dose—on which all authorities seem to agree—is 0.1 gm. For further information on the subject Gwathmey[2] refers us to some 174 contributions.

For solutions most commonly used see Appendix A.

III. General Technique.

1. *Preparation of patient.*

Elaborate preparation is, in my opinion, to be avoided: drastic or even excessive purgation and starvation are not only unnecessary, but definitely harmful. In the neurotic they increase the mental perturbation, and in the feeble, anæmic and cachectic they are a probable source of syncope and further debility. The patient should, as far as possible, be made to preserve a normal routine including meals etc., until some two hours before operation, unless the surgical procedure obviously precludes this, *e.g.*, carcinoma recti. I am in favour of giving some stimulant (particularly to the elderly)—strychnine, brandy, etc.—before what is to them an ordeal, because I believe that it increases their mental fortitude, improves their physical conditions, and cannot possibly do any harm.

2. *Premedication.*

I am definitely convinced that when spinal analgesia is employed, a preliminary injection of 1/6th grain morph. sulph.—1/100 hyoscine is beneficial. This calms the natural excitement of the patients; renders them more receptive of suggeston and in every way enables the anæsthetist to obtain a more complete control. The only possible objection to such an injection is that it tends to reduce the general metabolism and hence may increase the degree of shock. This lowering of general vitality I have to admit, but I believe that the advantages overcome the disadvantages to such an extent that I use it as a routine.

3. *Strict attention to surgical asepsis is essential.*

The skin over and around the area of injection should be prepared by shaving (when necessary), washing with soap and water, turpentine and a carbolic compress applied before the time of operation. Immediately prior to making the injection, I advocate the use of spirit in preference to any other disinfectant, *i.e.*, iodine, perchloride, picric acid, etc. These are all irritants and could conceivably be carried by the needle into the deeper tissues and provide a possible cause of local irritation. The skin over the site of injection is then frozen with an ethyl chloride spray and the needle directly inserted. In no case have I had any complaint of pain on penetrating the skin or deeper tissues when this was done. The syringe and needles used must be rendered aseptic by boiling in water, without the addition of soda (reasons previously given). The best needles for this work are made of irido-platinum in that they bend but do not break. They should have short points in order to minimise the risk of damage to the cord or cauda.

4. *Site of injection.*

I am aware that you all know the methods of locating the individual vertebral spines but would remind you that different authorities choose different levels at which to make the injection. Jonnesco[3] B.M.J. 1909 used a high injection in the mid-cervical region, but found that unpleasant phenomena—nausea, vomiting, pallor and temporary arrest of res-

piration followed. He now uses two sites, between 1st and 2nd dorsal and 12th dorsal and 1st lumbar. Ryall[4] uses 1st dorsal and 12th dorsal, but rarely the lumbar. Most other authorities inject through the lumbar spaces and rely on the specific gravity of the solution injected and the posture of the patient as the means of controlling the areas rendered analgesic. Even after puncture at the level of 4th and 5th lumbar space it has been stated on occasion to have become universal by extension upwards until on invovlement of the cerebrum the patient becomes unconscious and is apparently in a deep sleep —I am grateful never to have had a case which demonstrated this. In my experience lumbar injection is rarely followed by analgesia above the level of the umbilicus. Injection should not be made until a definite flow of cerebro-spinal fluid is obtained. Continued bleeding is another contra indication. Venous plexuses are more numerous on anterior wall of spinal canal. Puncture of nerve root causes sudden and sharp pain along the area of distribution. Puncture of cord causes no apparent reaction or pain as a rule.

Posture of Patient.

When I used Barker's solution I made the patient lie on the back with the head and shoulders raised a little and the pelvis slightly elevated, but since using a light solution I allow the whole trunk to be moderately inclined head downwards at the same time giving the patient a pillow in order to interfere with the comfort and ease of respiration as little as possible. I have found no objection to putting the patient in the Trendelenburg position (frequently extreme)provided it is done slowly and sudden changes in posture are not demanded—the influence of gravity on the cardio-vascular mechanism being very evident. Labat[5] advocates lowering the head to the horizontal immediately the needle is withdrawn, maintaining that it improves both respiration and circulation. Following all danger signals he recommends the Trendelenburg position.

Intercurrent Phenomena.

1. *Subjective.* Come on almost immediately, after injection, tingling and numbness of feet gradually extending up the legs and over the buttocks are followed by a feeling of

heaviness and numbness. Disordered sensations of heat and cold are sometimes noted. A feeling of general malaise, nausea, epigastric heaviness and sweating are other manifestations of the vasomotor upset occasionally recorded.

2. *Objective.* Impairment of pain sensation commences about 2—3 minutes after injection and analgesia is observed in feet, legs, perineum and abdomen successively. Loss of sensation to pain is followed by loss of touch and temperature sensations. The involvement of the motor system is evidenced by paralysis of the lower limbs and relaxation of abdominal muscles and demonstrated by loss of plantar, patellar and cremasteric reflexes. Extensors more markedly affected than flexors. The musculo-kinetic sense is also lost. The maximum effect is attained in 10 to 15 minutes and persists—in my experience— from 50 to 90 minutes. Paralysis of the sympathetic system allows the intestinal peristalsis to remain active and the uterus is stated to retain its contractibility.

3. *Vomiting* is occasionally seen during the analgesia. It usually commences some 10 to 20 minutes after the injection and disappears after a few minutes. The numerous authorities whom I have consulted express the most extreme differences in its incidence varying from 30 per cent. to nil. Personal observation leads me to conclude that it occurs seldom, is of short duration—I have never seen it persist through the analgesia. It has no apparent relationship to the amount of the injection and seems to be dependent on the fall in the general blood pressure. Traction on the mesentery and handling of the stomach appeared to cause it in some of my cases.

Post-operative Treatment.

Care should be taken in moving patient back to bed and patient should be kept perfectly still and lying flat for several hours. Some stimulant or hot drink is often advantageous as it relieves the thirst and obviates any feeling of nausea. Light diet may be ordered almost immediately unless the surgical procedure precludes it. Particular care should be taken that the patient is not burned before sensation is completely recovered and the bladder emptied by catheter if necessary.

Post-operative Sequelæ.

I have been perhaps exceptionally fortunate in that I have on two occasions *only* had to deal with any sequelæ, and one of these was, in my opinion, not directly due to the analgesia. I will give the cases in detail later.

Lack of personal experience, therefore, has forced me to review the literature of this section thoroughly, and given me considerable food for thought. The possible results are apparently both numerous and of the utmost gravity.

I. HYPERTHERMIA has been reported by Alessandri quoted by Bainbridge[6] and attributed to the action of the stovaine on heat centre. The temperature being as high as 104°F. Minor degrees of elevation of the temperature are of course common, not only in spinal analgesia but after inhalation anæsthesia and are, in my opinion, not due to the method.

II. INTENSE HEADACHE, generalized or confined to the occipital region are said to be comparatively common. My experience leads me to believe not nearly so common as supposed. In my series only five cases made any complaint even on enquiry.

Desplas[7] Headache, difficult to account for but present in his series of 260. 37, *i.e.*, 16 per cent., had cephalgia, 23 were transitory, but 14 were more intense and lasting—usually occurred alone and lasted from four to six days. In six cases it was accompanied by vomiting. Tennent R[8] (personal) Two cases in 139 series. One lasted two years, one lasted few weeks.

III. VOMITING is definitely reduced to the minimum and can justly be said to be rare. My cases four, none lasting more than 12 hours.

Desplas[7], Vomiting 29 in 260. 20 short duration occurring in first twelve hours. Three lasted for times up to 48 hours. In six for some five to six days. These were accompanied by other symptoms which to my interpretation appear to have the result of meningism.

IV. VARIOUS SENSORY DISTURBANCES AND PAIN ALONG NERVE TRACKS, are sometimes got, and are, I think, due to possible injury by the needle.

V. Motor Pareses. Most commonly the bladder and rectum are said to be affected but I again have not had an example, although my greatest number of cases have been for operations on the bladder and consequently that organ has been drained. Desplas agrees with me in that he had no cases of sphincteral disorder. Gray and Aitken[9] in personal communications inform me that retention of urine has been so troublesome that they use the method much less frequently than formerly, but regard it as the anæsthesia of selection for bladder and urethral cases.

Tennent in series of 139 cases had very few cases requiring catheterization.

Pareses of limbs, one or both, etc., but none of the writers enter into detail.

Ocular disturbances due to pareses of abducens, trochlearis and oculomotor are said to occur 4 to 18 days after, some 4 to 6 weeks. I have no experience. All pareses may become permanent.

Trophic lesions—bed sores and ulceration.

Psychic—insomnia to insanity. I cannot comment upon.

Meningism—syndrome: including pain in back, cephalalgia, vomiting, dizziness and cervical tenderness, probably due to mild cases of infection through faulty technique.

Albuminuria has been reported by some, but my experience agrees with that of Babcock[10] who failed to get any evidence of renal irritation.

Lusk[11] regards most after-effects as being the result of imperfect aseptic practice.

Pneumonia has been said to follow stovaine as often as inhalation anæsthesia; with this statement I do not agree. I have never seen a single case, and in view of the general condition of the patients to whom it is usually given, I feel bound to express grave doubts as to stovaine being in any way the causal factor. Desplas, however, records ten cases of pulmonary congestions and says "those prove spinal anæsthesia to be no protection against pulmonary complications," while Schultz[12] (Chicago) says "Post-operative pneumonias are reduced to a very low figure" which he attributes to the use of spinal in all cases having chest complications and no contra

indications. All cases of obstruction are also done under this analgesia in Lankenau Hospital.

In an interesting short article, Shapp[13] notes that nausea, faintness, sweating and pallor during the analgesia is much more marked in Europeans than natives (West African), and on the educated native more than his fellow. He gives the post-operative complications in order of frequency. Headache, backache, pyrexia, retention of urine, and injury to cauda.

Difficulties and Dangers and Treatment have already been mentioned as occurring in the analgesic period and post-operative. They may be summarized:—

1. Difficulties in making puncture due to spinal deformity: osteo-arthritis and partial ossification of the ligaments.
2. Failure to get flow—definite contra-indication.
3. Sepsis—faulty technique.
4. Vomiting and retching during the analgesia is said to be controlled most efficiently by oxygen administration. (Schultz).
5. Fall in blood pressure— most important. Adrenalin 20 minims. Caffeine 2 grains. Hypo. Ephedrine—best circulatory restorative. Labat—Regional Anæsthesia.

Caffeine	0.25 gm.
Spartein Sulph.	0.25 ,,
Sod. Benzoate.	0.30 ,,
Strychnine.	0.001 ,,
Aq. dis. ad.	2 c.c.s.

may be used subcutaneously as a preventative or on superven-tion of symptoms. In cases of failure of respiration he advocates its injection into the subarachnoid before artificial respiration is begun.

In those cases in which I supplemented the stovaine by a light ether anæsthesia, I was struck with the effect of ether and would now urge ether inhalation as a restorative.

The Trendelenburg position alone will often improve the condition of faintness and all authorities are agreed that it

should be adopted if the fall in blood pressure becomes extreme and in cases of complete collapse. Strychnine—used extensively by Jonnesco—I have never been able to persuade myself to have had any effect.

Adrenalin will undoubtedly raise the blood pressure, but it has a comparatively short effect. It acts most quickly when injected—5 to 10 minims to each 6 to ten ounces of saline—intravenously. I prefer to inject it subcutaneously and have found it of much use. On the supervention of marked depression the site of injection is massaged and in this manner a progressive absorption of the drug is assured. Given in this way I am of opinion that the effect is more sustained.

VI. Unilateral Analgesia, needle has not entered the cisterna terminalis and injection has been into or around the nerve roots of one side.

VII. Incomplete Analgesia, due to idiosyncrasy: deterioration of drug: use of alkali: faulty puncture, etc.

I do not advocate a second injection but prefer to supplement the first with general anæsthesia—gas and oxygen.

Indications for and against the use of spinal analgesia are exceedingly difficult to assess.

From the mass of literature on the subject I find that all shades of opinion are represented from those who can see no contra-indication to those who would have its use prohibited.

I, consequently, express my own opinion formed after consultation with the works of many writers and from experience. In general, I may thus express it:

Indications:

I. Those cases in which inhalation anæsthesia is contra-indicated, *e.g.*, pneumonia: pulmonary T.B.: bronchitic aneurism: pericarditis: uræmia: diabetes: senile gangrene and intestinal obstruction.

II. Conditions requiring an extreme degree of muscular relaxation or involving an unusual degree of shock—deep pelvic operations: rectal carcinoma: prostatectomy and other operations on bladder. In this latter group I regard it as almost essential to complete success.

Contra Indications:

I. All cases which before operation evidence any considerable degree of shock, from whatever cause.

II. All cases of cerebral or spinal disease.

III. Pyæmia.

IV. Operations above the level of the umbilicus.

V. All cases of advanced cardiac disease and those having a systolic blood pressure below 100.

SPINAL ANALGESIA.

Deaths: The following are given by Bainbridge.

Chiene	12,000 cases. (1 in 570)	22 deaths.
Strauss	22,717 cases. (1 in 498)	46 deaths.
Jonnesco	1,005 cases, 238 being high for operations on head, neck and thorax.	*No* deaths.
Kohler	7,780 cases. (1 in 649)	12 deaths.
Chaput	7,000 cases with *no* deaths.	
Bainbridge	1,065 cases with 1 death.	

I have no personal opinion to express.

CONCLUSIONS.

I. I believe that spinal analgesia by the injection of stovaine is, in selected cases, not only advantageous, but definitely indicated in the interest of the patient and surgeon.

II. That spinal injections are at least potentially dangerous and should not be used as a routine method.

III. Should not be regarded as a means to supplant inhalation anæsthesia, but rather to augment it.

IV. That the immediate mortality rate is low and the morbidity rate even after the most severe operations on debilitated but selected subjects, is also reduced.

V. That an anæsthetist should be present in all cases; should make the injection and be responsible for the general condition of the patient.

VI. That post-operative phenomena—paralysis, pareses, vomiting, headache, are rare.

VII. I have intentionally omitted any reference to the

psychic influences which may complicate any anæsthesia because of its extent and vagueness. The theories of the action of drugs injected into the cerebro-spinal fluid I have also avoided because they are at present non-conclusive.

Appendix A.

Solutions in common use :—

Bier :

Stovaïne	4%
Sod. Chlor.	0.11%
Epirenin borate	0.01%

Tuffier.

10% stovaine in normal saline.

Chaput.

Stovaine	10%
Sod. Chlor.	10%
Oxygen	80%

Stovaine Billon—dose 2 c.c.s.

Stovaine	0.04 gm.
Adrenalin	0.00013 gm.
Sod. Ch.	0.0011 gm.

Barker.

5% stovaine in 5% Glucose in sterile oxygen to 2 c.c.s.

Gray.

Stovaine 3% in dextrin and adrenalin.

Jonnesco.

Uses 0001–0.1 gm. of stovaine with strychnine.

Babcock.

Light solution.

(1) Stovaine 0.08 gm.
Lactic acid 0.2 c.c.
Alcohol 0.04 c.c.
Aqua 1.8 c.c.

Heavy solution.

(2) Stovaine 0.08 gm.
Lactic acid 0.04 c.c.
Lactose 0.10 gm.
Aqua 2 c.c.

Self.

Stovaine 0.04 gm.
Borate of Epinine 0.00013
Sod. Chlor. 0.0011
Sod. Chlor. 0.0011 per c.c. Dose 1–2 c.c.s.

Solutions should be fresh or drug may deteriorate.

Appendix B.

Series of 299 cases :—

Operative procedure.	*Number.*
Senile gangrene	16
Diabetic gangrene	19
Excision of Rectum	13
Prostatectomy	156
Other bladder operations	8
Hæmorrhoids	15
Gastrojejunostomy	2
Gall bladder	3
Herniotomy	44
Pelvic operations	10
Varicose veins	8
Appendix	5
Total	299

Results :

One complete failure to get any analgesia.

Five incomplete analgesias requiring the administration of gas and oxygen anæsthesia.

In 167 cases Stovaine was given alone with complete success.

In 15 cases Stovaine plus light ether anæsthesia and in 79 cases plus nitrous oxide plus oxygen anæsthesia.

The mixed analgesias and anæsthesia were used by election and not of necessity.

No death : no after effects, except vomiting in 3 cases and headache in 5.

Appendix C.

Case. I. Post Operative Syncope.

Half an hour after the completion of the operation patient shewed sudden collapse—I regret I had left hospital. When seen by the surgeon he was extremely pallid and pulse and respirations were almost imperceptible. Injections of caffeine and ether and vigorous artificial respiration were resorted to and patient shewed marked improvement in some ten minutes. He made a complete recovery. Stovaine used alone. Patient was a man over 60 years of age with marked arterio-sclerosis, chronic bronchitis and enfeebled by carcinoma recti. At operation the rectum was excised—time 1 hour 35 minutes—and there was very considerable loss of blood.

I believe the collapse to have been as much due to hæmorrhage as to the injection.

Case II.

Woman—aged round about 40—operation myomectomy and ovarectomy. General condition of patient good, and anæsthesia was gas and oxygen plus 1 c.c. spinal injection containing 0.05 gm. Stovaine.

Complete loss of motor function of lower limbs quickly followed injection but abdominal muscles did not relax either immediately or later. Analgesia on limbs and buttocks was perfect but over the abdomen poor. Following day patient complained of intense headache and visual disturbances—both distortion of object and diplopia.

On examination—I found all sensations—pain, touch, temperature, normal in legs. Motor power was completely recovered. Bladder and rectal control and function perfect. Eye condition certainly not due to impairment of action of any of the muscles. Movements of eyeballs in all ranges being complete. Areas of double vision were *not* constant, and on my suggestion straight lines became "wavy." Diplopia was never constantly present. Patient was known to be neurotic and regarded herself as "different to other patients." The visual phenomena disappeared on the third day, but headache was still complained about. Patient refused to take any drugs to remove headache because "she could not take opiates."

It is worthy of note that all symptoms were subjective but I have little doubt that the headache was due to the stovaine injection.

REFERENCES.

1. Dandy. *Annals of Surgery*, 1919.
2. Gwathmey. " Anæsthesia."
3. Jonnesco. *B. M. J.*, 1909.
4. Ryall. *B. M. J.*, 1909.
5. Labat. " Regional Anæsthesia."
6. Bainbridge. "Gwathmey's Anæsthesia."
7. Desplas. " Spinal Anæsthesia and it Drawbacks," *Lancet*, 1923.
8. Tennent. Personal communication.
9. Gray and Aitken. Personal communication.
10. Babcock. *Penn. Med. J.*, 1909.
11. Lusk. *Annals of Surgery*, 1911.
12. Schultz. *Surg. Gyn. & Obst.*, 1928.
13. Shapp. *West African Med. Journ.*, 1928.

OBSERVATION ON THE BLOOD SUGAR CHANGES IN GENERAL ANÆSTHESIA

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THE object of this work, which is part of an investigation into the variations of certain blood constituents during the course of general anæsthesia, is to indicate (*a*) the changes in the blood sugar level in general anæsthesia (*b*) how these changes may be influenced by small doses of insulin and (*c*) the course followed by the blood sugar when a local anæsthetic is administered in addition to a general anæsthetic in a major operation involving laparotomy.

Method of Investigation.

A total of 71 cases for operation under general anæsthesia was investigated. Apart from the elimination of known diabetics and glucosurics, and of cases where the operation was expected to be of short duration, the cases were not selected in any way. About half of the cases were women. Ages varied from 9 years to over 70 years. About 90 per cent. were cases of chronic as opposed to acute disease. The types of diseases were representative of those found on the surgical side of any large general hospital.

Pre-operative Procedure.

The preparation of each patient for operation, as regards rest, diet, laxatives, etc., was practically uniform. Most of the operations were performed in the morning. Venupuncture at the elbow was carried out just before the induction of anæsthesia, and at intervals of about 20 to 25 minutes during the period of anæsthesia, and, in some cases, also after anæsthesia, all time intervals being carefully noted. The blood sugar estimations were all carried out on the same day by MacLean's method (1925).

Anæsthesia.

Generally either chloroform-ether mixture throughout, or induction by CE mixture followed by ether alone, by either an open or closed method, was favoured by the different anæsthetists. A few cases received oxygen in addition. Practically all cases received atropine 1/100th gr. and more than half received morphine 1/6th gr. before operation. Observations throughout the whole series failed to demonstrate any significant difference, so far as blood sugar changes were concerned, between those types of anæsthesia, or between those patients who received and those who did not receive a preliminary dose of morphine.

The first 26 cases received no insulin, the next 37 received 10 units of insulin just before the administration of the anæsthetic, and the remaining 8 cases, which all necessitated laparotomy, received, in place of insulin, an injection of 30 ccs. ½ per cent. novocaine into the abdominal wall in the site of the proposed incision, and, when the nature of the disease and of the operation warranted it, (*e.g.* gastro-enterostomy for certain chronic gastric ulcers) a further 70 ccs. into the coeliac plexus to obtain splanchnic anæsthesia. In a number of cases the operation was completed in less than 30, or less than 60 minutes, and these have necessarily been omitted from certain of the calculations in the different groups.

All the data relevant to each case were carefully noted—name, age, sex, obesity, cachexia, disease, operation, preliminary sedatives, salines, etc., the presence or absence of such factors as preliminary struggling, cyanosis, collapse, hæmorrhage, etc., the times of taking blood samples, the length of the period of anæsthesia, the results of the urinary analysis before and after anæsthesia. Blood sugar curves have been drawn up for each case, but considerations of space here permit only of the demonstration of the average figures obtained from each group.

Results.

The results obtained for the different groups are as follows:—

Group A. Anæsthesia for minimum period of 30 minutes.

The first 20 cases received no insulin, the next 30 received 10 units of insulin before anæsthesia.

No. of cases	Average °/₀ B.S. before operation	Average °/ B.S. after 30 mins. anæsthesia
20 (no insulin)	0.106	0.149
30 (10 units)	0.110	0.157
Increase in 30 mins. in non-insulin group		=0.043%
,, ,, ,, ,, ,, insulin ,,		=0.047%

Group B. Anæsthesia for minimum period of 60 minutes. The first 12 cases received no insulin, the next 18 received 10 units of insulin before anæsthesia.

No. of cases	Average °/₀ B.S. before operation	Average °/₀ B.S. after 30 mins.	Average °/ B.S. after. 60 mins.
12 (no insulin) ...	0.112	0.155	0.216
18 (10 units) ...	0.103	0.148	0.172
Increase in 60 mins. in non-insulin group			=0.104%
,, ,, ,, ,, ,, insulin ,,			=0.069%

Group C. In certain cases, although anæsthesia was not maintained for more than 45 minutes, blood sugar observations were taken frequently until about four hours from the beginning of the operation. The following figures are those derived from all the cases in the insulin and non-insulin series whose period of anæsthesia lasted from 35 to 50 minutes. The average duration for the non-insulin series was 40 minutes, and for the insulin series 43 minutes, which is approximately equal.

Time intervals	Average °/₀ B.S. for 9 cases. No insulin.	Average °/₀ B.S. for 8 cases. 10 uuits insulin.
Before operation	0.104	0.101
After 50 minutes	0.167	0.149
,, 100 ,,	0.163	0.150
,, 150 ,,	0.162	0.143
,, 200 ,,	0.160	0.136
,, 250 ,,	0.152	0.129

Group D. Eight cases were examined in which a local anæsthetic, ½ per cent. novocaine, was employed in addition to the ether or CE mixture. They each received 30 ccs. novocaine solution in the site of the incision and 70 ccs. under the peritoneum in the region of the coeliac plexus. None received insulin. In every case anæsthesia lasted for over 90 minutes. As the figures obtained are of interest they are shown in full below.

Case No.	% B.S. before operation	% B.S. after 30 minutes	% B.S. after 60 Minutes	% B.S. after 90 minutes
S 1	0.165	0.172	0.210	0.215
S 2	0.112	0.142	0.120	0.100
S 3	0.095	0.122	0.138	0.144
S 4	0.106	0.231	0.193	0.162
S 5	0.086	0.120	0.145	0.156
S 6	0.084	0.124	0.140	0.134
S 7	0.075	0.090	0.100	0.106
S 8	0.093	0.110	0.137	0.120
Average	0.102	0.139	0.148	0.142

Further results obtained from analysis of all the cases may now be indicated.

1. The percentage of sugar in the blood was found to increase in 69 out of the 71 cases examined during the course of ether or chloroform-ether anæsthesia, *i.e.* in 97 per cent. of cases.

2. The increase in the blood sugar tended to be continuous and progressive in cases of anæsthesia up to 60 or 90 minutes. The average increase in 30 minutes was found to be 0.043 per cent. (20 cases), and in 60 minutes to be 0.104 per cent. (12 cases). Where the initial blood sugar was low the increment tended to be above this average, and where it was high the increment tended to be below the average.

3. In anæsthesia lasting up to one hour the maximum point in the blood sugar curve usually occurred about the end of anæsthesia.

4. The rate of fall or of return to normal of the blood sugar curve was considerably slower than the rate of the initial rise.

5. When 10 units of insulin were given immediately before the anæsthetic (20 cases) the blood sugar increased by 0.047 pre cent., the comparable figure for the non-insulin series (30 cases) being almost the same, *viz.* 0.043 per cent. In the second half-hour of anæsthesia, where 10 units of insulin were given, (18 cases) the increase was 0.024 per cent. compared to the marked increase of 0.061 per cent. in 12 non-insulin cases.

6. In 8 cases out of 37 in which insulin was given, the maximum point of the blood sugar curve occurred during the course of the anæsthesia, *i.e.* before the end of anæsthesia a fall in the blood sugar was setting in.

7. General observations on the patients, on the ease or otherwise with which they stood the strain of the operation, and on their clinical condition after the operation, revealed no essential difference between those who had received the 10 units of insulin and those who had not. In the cases where splanchnic anæsthesia was employed the absence of severe post-operative shock was a notable feature.

Discussion on the Results.

It was not possible to differentiate clearly the effects of maintaining the anæsthesia by ether alone as compared with CE mixture, but an examination of individual cases, however, conveyed the impression that, so far as the blood sugar changes were concerned, there was no essential difference between the two types of anæsthesia.

A marked rise in the sugar content of the blood appears to be the usual accompaniment of general anæsthesia. The rate and extent of the rise in 40 minutes anæsthesia is very similar indeed to that consequent on giving a test meal of 50 gms. glucose, but the rate of return to normal is considerably slower.

The apparently greater increase in the second half-hour of anæsthesia is due, doubtless, to the fact that it takes 5 to 10 minutes, according to the length of the period of induction, before any rise becomes apparent in the early stages of anæsthesia.

A small dose of insulin, such as 10 units, given just before anæsthesia, had no effect on the blood sugar in the first half

hour but the diminution in the extent of the increase was quite well marked in the second half hour. This naturally suggests that to be effective in the induction period insulin should be given at least half an hour before the anæsthetic. A study of several of the cases showed that if given after the hyperglycæmic process had set in, insulin had no effect in checking it, at any rate in 10 unit doses.

An examination of the figures obtained in Group D, where the local anæsthesia was employed in addition to the general anæsthetic, is interesting. It will be noticed that, even when the slight differences in the average initial blood sugar are taken into account, the course followed by the rising blood sugar in this group remains lower, not only actually, but, which is more important, also relatively, than in the group where no local anæsthetic is employed. This difference is still more definitely accentuated when it is noted that the period of anæsthesia in this group was at least 90 minutes (and therefore a very great increase in the blood sugar was to be expected) while the periods for comparison in the earlier groups with no local anæsthesia was only 45 and 60 minutes. The injection of the novocaine was therefore more effective than 10 units of insulin as here administered in retarding the rise of the blood sugar. In this connection it may be mentioned that Epstein and Aschner (1916) have demonstrated that no rise in the blood sugar occurs when a local anæsthetic is employed without a general anæsthetic. The explanation suggested for this probably resides in the fact that considerably less ether or CE Mixture is necessary to keep the patient under when the combination of anæsthesias is employed. By this method Dr. Somerset has been able to maintain anæsthesia for as long as two and a half hours using only five ounces of ether. At present, it is customary to precede anæsthesia in operations on diabetics with varying-doses of insulin. The foregoing figures clearly suggest that in such cases it would be worth while employing also a local anæsthetic in addition, where the operation involves laparotomy and is likely to last over half an hour. By such means the risk of hyperglycæmia, so often the prelude to coma in diabetes, might be considerably minimised.

While the foregoing observations offer no explanation of the rationale of the hyperglycæmic process, it is at least

interesting to speculate on the mode of occurrence. It is suggested that ether and chloroform act as tissue poisons, with a special action on the liver. They have the effect, probably quite indirectly, of breaking down the stores of glycogen in the liver and the muscles, and mobilising the resulting glucose in the blood. Whether this increase in the blood sugar is to be regarded as protective in nature or not, is difficult to say. The figures for certain of the cases certainly show that hyperglycæmia over 0.180 per cent. is not essential for obtaining anæsthesia. Case No. S7 (see Group D) shows that anæsthesia may we maintained for 90 minutes without the blood sugar exceeding 0.106 per cent. On the other hand marked hyperglycæmia is not necessarily harmful as at least 12 of the cases in the whole series had a maximum concentration of over 0.240 per cent.

SUMMARY.

An investigation into the blood sugar changes in general anæsthesia shows that, as anæsthesia proceeds, the blood sugar rises steadily, the average increment being about 0.045 per cent. in the first half-hour, this figure being increased by about 0.061 per cent. in the second half-hour. These increases may be diminished by the injection of insulin previous to the administration of the anæsthetic. They may be also considerably decreased by the simultaneous use of a local anæsthetic such as novocaine in long abdominal operations, a proceeding of value when operating on diabetics, or on cases where shock is to be anticipated.

This investigation has been carried out in the Biochemical Laboratory of the Wolverhampton and Staffordshire General Hospital by kind permission of Dr. S. C. Dyke, Pathologist to the Hospital. I am indebted to Mr. Deanesly, B.Sc., F.R.C.S., and Mr. Cholmeley, F.R.C.S., Honorary Surgeons to the Hospital for the facilities accorded me in their theatres and wards, and to all the members of the anæsthetics staff for their cordial co-operation. I have to thank the Council of the British Medical Association for a Grant towards the expenses of this research.

REFERENCES.

Epstein, A. A., and Aschner, P. W. (1926) *J. Biol. Chem.* 25, 151.

Maclean, H. (1925) "Diagnosis and Treatment of Glycosuria and Diabetes."

CONTROLLABLE SPINAL ANÆSTHESIA, "SPINOCAINE."

(Metz).

By GEORGE P. PITKIN.

FOR several years I have been using Spinal Anæsthesia as described by various operators endeavouring to obtain an isotonic solution. The results were more or less unsatisfactory which lead to a series of experiments and investigations with the endeavour to overcome a tremendous drop in blood pressure, to prevent pallor and cold sweats, to minimize the amount of nausea and vomiting, to eradicate post-operative shock and headache and to eliminate post-operative complications. What has been accomplished in this line is well shown in the thirty-one hundred (3100) inductions by myself and associates and nearly six thousand (6000) additional anæsthetics performed by various men in the United States. We have found that we are able to avoid all the unpleasant phenomena of Spinal Anæsthesia.

The blood pressure may be maintained or increased, to any desired degree as the operator chooses. Pallor and cold sweats never occur, nausea and vomiting does not present in more than one or two per cent. of the cases, post-operative headaches are exceedingly rare and when they do occur they are mild. Post-operative complications are almost an unknown quantity. Occasionally they spring up, but when they do they may be traced directly to improper technique.

By experiment we have attempted to establish the time of absorption of the anæsthetic agent, the intra-dural irritability, the elimination time, the relation between the intra-dural and intravenous pressure and by the use of the gliadan we have concocted a solution of such viscosity that it will not mix or disseminate with the spinal fluid until such a time as the anæsthetic agent has been absorbed. The solution is of a lighter specific gravity and will float upon the spinal fluid, not unlike the air bubble on the spirit level.

By our ability of controlling the anæsthetic, we are also able to regulate the time of the anæsthesia. The nature of the solution is such that the toxicity of the drug is reduced, or, in other words the absorption is rendered so slow that two hundred (200) milligrams or even four hundred (400) milligrams of novocaine may be introduced into the sub-arachnoid space without producing as many toxic symptoms as if one hundred (100) milligrams was dissolved in the spinal fluid and re-introduced.

THE EFFECT OF ANÆSTHETICS ON THE RED BLOOD CELLS.

By W. Webster, M.D., C.M.

From the Gordon Bell Research Laboratory, University of Manitoba Medical School.

IT has long been supposed that at least some of the anæsthetics in common use had a destructive effect on the red blood cells of the body.

It appeared desirable, therefore, to inquire whether there was any sufficient basis for this supposition and if so, the extent of the damage done, and whether all or only some of the anæsthetics in common use were responsible.

The anæsthetics examined in this regard were nitrous oxide, ethylene, ethyl chloride, chloroform and ether.

A priori one would expect that such anæsthetics as chloroform and ether—which are lipoid solvents—would be the most destructive, as the framework of the red cell is composed largely of this material in which the hæmoglobin is deposited.

It was considered best that these experiments should be conducted on the human subject, therefore, each specimen of blood examined was so obtained. Clotting was prevented by the admixture of a few drops of potassium oxalate. A control portion of each specimen was examined as taken from the body, the remainder was examined after exposure to the vapour of the anæsthetic effected by passing this through the blood in small bubbles for various periods of time. In spite of the care exercised in conducting these experiments it was felt that, at least some of the resulting hæmolysis might be due to mechanical causes such as the movement of the cells caused by the gases passing through the liquid, which would obviously vitiate the experiment, making it worthless. It was suggested that one might take a constant for this by estimating the destruction which occurred when

air only was passed through the specimen for an equal period of time. This method proved also to be unreliable and it was finally determined to obtain the specimen from the patient, before and after exposure to an anæsthetic, in the ordinary course of an operation.

The usual care was exercised to prevent hæmolysis while taking each specimen—of which at least 10 c.c. were required for the necessary examination—to exclude entrance of air with the blood by, in the first place using a reliable make of syringe, then by securing a complete vacuum with the application of a little vaseline to the plunger and at the junction of the needle with the syringe.

The first specimen of blood was taken shortly before the commencement of anæsthesia, the second, immediately on completion of the operation before the patient left the operating room. Later, for reasons which will be shown, a third specimen was taken at a varying time after withdrawal of the anæsthetic.

The method of examination adopted was to count the red blood cells in each specimen. On another portion make an estimation of the bulk of the red corpuscles by centrifuging a specimen in the hæmatocrit at 3,000 revolutions per minute. A further 1 c.c. of the blood was diluted 200 times with decinormal hydrochloric acid and after standing one hour the hæmoglobin estimated by the Duboscq colorimeter against a standard 1-200 dilution of human blood, containing approximately 100 per cent. of Hb.

Another portion of the original blood was centrifuged at 3,000 rev's., the plasma drawn off, mixed with equal parts of 2 per cent. HCl, and examined with the colorimeter using the same standard as above.

Plate I shows the method of arriving at the quantity of Hb. by the Duboscq colorimeter.

The specimen of blood used as a standard contained 11.2 grams. Hb per 100 c.c.

Diluted 1-200 = .056 gram. Hb. per 100 c.c. of solution.

Serum diluted 1-2 with .2% HCl.

$5/11 \times .056 \times 2 = .56/11 = .051$.

$5/9.8 \times .056 \times 2 = .56/9.8 = .057.$
$5/8.6 \times .056 \times 2 = .56/8.6 = .065.$

Whole blood. $\frac{11.2 \times 5}{3.3} = \frac{56}{3.3} = 16.8$ grams. Hb. %.

This gives up to the serum during anæsthesia .006 gram. Hb. per 100 c.c. serum.

This is liberated from 40 c.c. cells to 60 c.c. of serum.

So that 60 c.c. will contain $60/100 \times .006 = .0036$ grams.

In % $\frac{.0036}{16.8} \times \frac{100}{1} = .0215.$

Plate II.

Ether semi-open 50 minutes.

Whole blood dil. 1-200 with N/10 HCl.	Before Anæsthesia		After Anæsthesia		4—5 hrs. later	
Vernier scale of colorimeter containing Standard solution set at 5 m.m.	Colorimeter reading 3·3 mm.	Hb. in 100 cc. of blood 16·8 gr'ms	Colorimeter reading 3·2 mm.	Hb. in 100 cc. of bloo 17·5 gr'ms.	Colorimeter reading 3·45 mm.	Hb. in 100 cc. of blood 16·2 gr'ms.
Blood plasma diluted with an equal part of ·2% HCl.		Hb. in 100 cc. pl sma		Hb. in 100 cc. pl'sma		Hb. in 100 cc. pl'sma
Standard of Colorimeter at 5.	11	·051 gr'm.	9·8	·057 gr'm.	8·6	·065 gr'm.
Hæmatocrit reading.	40		40		—	
Red blood cells.	5·733·000		5·422·000		5·466·000	
% Hb. liberated.	·0215		·027		·029	

Ethyl Chloride. 35 minutes. Semi-open .

	Before Anæsthesia.	After Anæsthesia.
Whole blood. Hb.	.057.	.077.
Plasma Hb.	.07.	.075.
Vol. cells, hæmatocrit. ...	37.	37.
Red cell count.	4.988.000	5.122.000.

Chloroform. 25 minutes.

Whole blood. Hb.	.05.	.05.
Plasma. Hb.	.055.	.067.
Vol. cells, hæmatocrit. ...	34.	33.
Red cell count.	4.005.000.005.000.	3.933.000.

Ethylene. 35 minutes.		
Whole blood. Hb.	.013.	.014.
Plasma Hb.	.112.	.119.
Vol. cells, hæmatocrit. ...	37·5.	——
Red cell count.	4.355.000.	4.250.000.
Nitrous oxide. 40 minutes.		
Whole blood. Hb.	.042.	.041.
Plasma Hb.	.04.	.045.
Cell Vol. hæmatocrit. ...	26.	25.
Red cell count.	4.033.000.	4.122.000.

The above are examples from a series of 26 experiments and show approximately the average of results.

The very slight difference in hæmoglobin content between the plasma of blood before and after use of the above anæsthetics is within the limit of error. In fact, the small fraction of difference is about as often less as it is more than before anæsthesia. It, therefore, appears that, although when in sufficiently long contact with blood as they may be in experiments outside the body, these anæsthetics will cause hæmolysis, still in the concentrations and quantity used for the purposes of anæsthesia in the human subject the damage resulting to the red blood cells is inappreciable and may be ignored.

It was thought possible that, especially in the case of those anæsthetics slowly eliminated, their more prolonged contact with the blood might produce hæmolysis later and, to test this phase of the subject, further specimens were taken at intervals of from 2 to 8 hours after withdrawal of the anæsthetic without obtaining any markedly different results. The bulk of chloroform and ether vapour is eliminated within 45 minutes after anæsthesia, only small and decreasing percentages remain up to 7 or 8 hours; *e.g.* the quantity of chloroform in arterial blood which causes the beginning of anæsthesia is from 30 to 40 m.g. per 100 c.c. of blood; the quantity which produces absolute anæsthesia is 40 to 50 m.g. per 100 c.c. Five minutes after administration ceases half the quantity in the blood is eliminated, after two hours the quantity remaining is about 4.9 m.g. per 100 c.c. of blood.

After 7 hours it has nearly, if not entirely disappeared. The time of ether elimination approaches closely that of chloroform.

In the case of ethyl chloride the quantity required to produce anæsthesia varies in different subjects from 30 to 150 m.g. per 100 c.c. of blood. Elimination is, however, very rapid, in 5 minutes nearly all has disappeared from the blood, none has been found after 10 minutes.

Nitrous oxide is eliminated in about two minutes, therefore one would expect that any damage resulting from this anæsthetic would show immediately on completion of anæsthesia.

Ethylene is somewhat slower of elimination than nitrous oxide, but is sufficiently rapid that any injury resulting to the cells would probably show by the completion of anæsthesia.

A further question occurs. Is the volume of the red cells increased by absorption of the anæsthetic? It is well known that anæsthetics are not all absorbed in equal ratio by the red cells and plasma. The red cells during anæsthesia contain 9 parts of chloroform to one part contained in the plasma. The other anæsthetics are distributed more evenly between the cells and the plasma, nitrous oxide being almost equally absorbed between them.

If there were any increase in bulk of the red cells one would expect it to show most after the administration of chloroform. The cell volume, as shown by the hæmatocrit, is practically unchanged by the absorption of this anæsthetic as with the others used. We may, therefore, assume that absorption of anæsthetic vapours, in the quantity necessary to produce surgical anæsthesia does not appreciably increase the size of the red blood cell.

My thanks are due to Professor Cameron of the Department of Biochemistry for his invaluable advice and criticism during the progress of the above research.

ANÆSTHESIA FROM THE STANDPOINT OF THE BIOCHEMIST *

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I shall discuss briefly the various phases of the art of anæsthesia that particularly interest me as a chemist. The specialist in anæsthesia has extended his interest from the technical procedures of administration to the fundamental chemical, physiologic, and pharmacologic basis of the art, including the abstract subject of structural organic chemistry with its complexity of atomic arrangements. Perhaps the majority of organic chemists at some period in their careers synthesize substances which present possibilities of use as hypnotics or anæsthetics, but the fact that the ideal anæsthetic agent for routine use remains as yet unknown serves as a stimulus for further constructive synthetic investigations. Many comparatively unrelated series of organic substances have been developed, since even with our present extensive knowledge of the structural relationships of the organic substances that may be used as local anæsthetics, but little can be accomplished in the prediction of the variations in physiologic response which may be expected from the rearrangement of the structural relations of the atoms within the molecule. At present only a few simple generalizations are known which guide the organic chemist in his endeavours to synthesize better hypnotics and anæsthetics, and these apply in the main to homologous series of compounds.

We owe the greater part of the present successful development of local anæsthetics to our knowledge of the structure of the cocaine molecule. The tropin series, the piperdine

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derivatives, and the procaine family of substances owe their existance to knowledge gained from a study of the structure of the cocaine molecule. Numerous organic substances have been synthesized which vary only slightly in structure but which are considerably different in anæsthetic potency and in toxicity.

Reasoning from the Meyer-Overton theory of narcosis it would seem that the anæsthetic ability of a substance is dependent more on its physical properties than on its structure, conceding naturally that physical properties are somewhat dependent on organic structure. Thus hypnotics which are optical isomers of one another and so differ in their structure, but which have identical physical properties, should have the same hypnotic ability. This has been found to be true with certain barbituric acid derivatives. The dextrorotatory, the levorotatory, and the racemic forms of ethyl, secondary octyl barbituric acid do not differ in their hypnotic effect. Isomers, however, such as cocaine and alpha cocaine which differ in their physical properties as well as in their structure, because of the shifting of an organic group from one atom to another, are decidedly different in their ability to produce anæsthesia. The equality of physiologic response of an organism to optical isomers is not true of such a compound as epinephrine the dextrorotatory and levorotatory forms of which differ considerably in their action.

Differences are noted in the degree and rapidity of response of sensory and motor nerve fibres to various drugs and to physical treatment. The substances cocaine, B. eucain, butyn, and procaine paralyze the sensory fibres first, and apothesine affects the motor fibers first. Heat and desiccation simulate the properties of local anæsthetics by affecting primarily the sensory fibres.

In general, local anæsthetics are organic bases and as such are soluble in lipoids and organic solvents. For purposes of aqueous solubility and for administration, however, acid salts are used. These salts per se are ineffective as anæsthetics and require neutralization by an alkali, such as sodium bicarbonate or by the alkaline tissue fluid, to liberate the free base which is lipoid-soluble and effective as an anæsthetic. The liberation of the free base by neutralization of the acid salt with

alkali increases absorption and may be beneficial in anæsthetizing the eye or tongue. Neutralization lessens the time required for the production of a nerve block or the time of recovery of an exposed nerve, but for injection purposes, when alkaline and buffered tissue fluids are encountered, it is of no material help.

Attempts to potentiate the action of procaine by the simultaneous administration of other local anæsthetics result only in a summation effect on motor or sensory nerve block. The question of potentiation or the synergizing power of one drug on another is becoming of increasing interest. The synergizing action of magnesium salts in morphine and other anæsthesia and the neutralization ability of calcium salts on the paralyzing properties of the magnesium ion become of considerable scientific interest. The explanation can probably be found in experimental observations of the effect of these salts on emulsions of water and oil. It is well known that sodium salts, such as sodium oleate, produce an emulsion of oil surrounded by a continuous phase of water by reason of the fact that the sodium ion lessens the surface tension of water to the extent that its surface assumes a concave shape allowing the oil to form into droplets. On the other hand, calcium or magnesium oleates, being more soluble in oil than in water, allow the aqueous phase to maintain a higher surface tension than oil so that its surface remains convex, forming droplets of water suspended in a continuous oil phase. A system having a continuous aqueous phase has a much higher electrical conductivity than one with a continuous oil phase, and in the latter condition there is a smaller molecular interchange between the external medium and the interior of the cell.

It would seem that anæsthetic action is dependent on the nature and the permeability of the surface layers surrounding the nerve cells. In a physiologic state or in a solution such as Ringer's, which is somewhat comparable in its ionic composition to that of a living cell, both types of emulsion may exist. To maintain this state of equilibrium the ratio of sodium to calcium ions must remain approximately the same as that existing within the cell, namely a ratio of 25 to 50 sodium ions to each calcium ion. Although both calcium

and magnesium as divalent elements react antagonistically to sodium and reverse the type of emulsion, they also act antagonistically to each other under certain conditions of concentration. This phenomenon is due to the relative solubility of magnesium and calcium oleates in oil, magnesium oleate being much more soluble. An-oil-in-water solution produced by sodium oleate is reversed to a water-in-oil system by the addition of a small amount of magnesium chloride. The addition of a small amount of calcium chloride will result in a much higher proportion of a continuous water phase containing droplets of oil. If the normal state of the surface layer of the cell is dependent on a certain concentration of inorganic ions, any excess of such an ion as magnesium would tend to produce a predominance of a water-in-oil system in the surface layer. Such a system would theoretically favour the production of an anæsthetic or analgesic state because of increased lipoid solubility, a decreased interchange of inorganic ions, and a decreased electrical conductivity. This has been shown to be true of ordinary soporific drugs and analgesics which in vitro produce water-in-oil emulsions. Magnesium sulphate applied to a nerve trunk decreases excitability, lessens or blocks conductivity and, by recent studies, has been shown to synergize the action of certain antipyretics.

Regardless of the mechanism that exists for the production of anæsthesia, the fact seems certain that a state of narcosis must be dependent on a certain concentration of the drug in and around the cells which are to be anæsthetized. Hence, a fundamental problem of anæsthesia concerns itself with the production of this concentration of the narcotic. The concentration of the drug may be measured directly in grams for each unit volume of blood or tissue or, in the instance of a gas, in the percentage of tension of the respired air which it exerts when in equilibrium with a particular fluid. For example, the concentration of ether within the blood stream during anæsthesia is 120 to 150 mg. for each 100 c.c. of blood, or, expressed in other terms, the tension of ether in the respired air which is in equilibrium with the circulating blood of the lung during anæsthesia is found to be 3.5 per cent. Hence the ratio for each unit

volume of ether in the blood to that in the respired air is 15.1.

Absorption of ether is dependent on the mode of administration and is mainly through the lungs or by way of the alimentary tract, so that the laws governing its absorption are naturally different. Absorption from the respired air through the lungs depends on the distribution ratio of ether as a gas between air and blood and in solution between blood and tissue, whereas its absorption from the colon is dependent on the distribution ratio of ether in solution between oil and blood and between blood and tissue. The equilibrating forces responsible for the passage of ether from air to the body and from body to air depend on the portion of the atmospheric pressure which it exerts. The pressure of the various gases which constitute the atmosphere, each gas exerting its own particular percentage of the total pressure, is equivalent to 760 mm. of mercury at sea level. For example, oxygen is responsible normally for approximately 21 per cent. and the tension exerted by ether in the respired air during constant ether anæsthesia is about 3.5 per cent. of the total gas pressure.

Ether is a stable chemical entity and passes through the organism unchanged. Approximately 90 per cent. of absorbed ether is excreted by means of the respiration, but a small amount is present in the secretions of the body, appearing in the urine at the time of its excretion in the same concentration as that which is present in the arterial blood. The average solubility of ether throughout the organism is roughly equal to that of the blood, but a consideration of only nerve tissue shows a greater degree of solubility so that during the state of anæsthetic equilibrium, ether is present in nerve tissue in a greater concentration than in the remaining tissues of the organism. The central nervous system is the seat of action of general anæsthetics for the production of unconsciousness and the loss of function of the sensory nerves. This system constitutes only about five per cent. of the total body weight, so of necessity the drug distributes itself between a small amount of tissue where it exerts the desired physiologic action and a large amount of tissue on which, so far as anæsthesia is concerned, its effect is unimportant. The maximal concentration of ether

in any tissue is dependent on the solubility of the drug in that particular type of tissue, and the rate at which the tissue reaches saturation is dependent on the rapidity at which the drug may be brought to the organ. The latter effect is controlled by the flow of the blood supply and the distribution coefficient of the drug. Thus the brain which has a liberal blood supply and a comparatively high solubility coefficient for ether reaches its saturation point much more rapidly than the remainder of the organism. A close correlation, therefore, exists between the concentration of ether within the brain and the concentration of ether in the arterial blood. The solubility of ether is approximately the same in arterial blood and in nerve tissue, so that all tissues, including the brain, during ether anæsthesia have a lower concentration of ether than arterial blood. Ether anæsthesia produces hyperglycemia which simulates that of diabetes mellitus and which can be prevented by the appropriate use of insulin previous to the induction of anæsthesia. Simultaneously there is a rise in the total fat content of the blood with the total cholesterol bodies playing a part in this lipemia. The rise in cholesterol is prevented also by the administration of insulin so there would seem to be a definite parallelism between the hyperglycemia and the hypercholesterolemia due to suppression of the pancreatic activity.

Much contradictory evidence exists in the literature regarding the question of acid-base balance during general anæsthesia. This is not so much because of inaccurate experimental work, as because of the many variables encountered in the production of and in the state of anæsthesia and in the unreliability of the direct transference of conclusions drawn from the production of a simple anæsthetic state in an animal to the physiologic state of a patient under anæsthesia during a surgical procedure. Without reviewing the vast amount of work in this subject, it is established that anæsthesia such as that produced by ether or nitrous oxide results in marked acidosis, and when this anæsthesia is complicated by trauma, muscular movements, and possibly sensory stimulation the acidosis is more pronounced. If the method of administering the anæsthetic includes rebreathing or the administration of carbon dioxide, the carbon dioxide tension of the blood may be further increased with

a consequent higher hydrogen-ion concentration. Under these conditions the sensitiveness of the respiratory system may be decreased so that a higher concentration of carbon dioxide than normal is required to obtain increased ventilation. Increase is not noted in acetone bodies or lactic acid, and the previous impression that increased elimination of phosphates takes place which might explain the drop in blood alkali is open to question in the light of later work. In non-complicated light ether, ethylene, chloroform, urethane, and chloretone anæsthesia there is depression of inorganic phosphates of the blood as well as phosphate excretion in the urine. The recovery period is followed by a rise of the blood phosphates and an increased phosphate excretion which, however, does not reach its fasting level for several hours. In pancreatectonized animals the variation of phosphate values is not encountered, suggesting the possibility of a connection between glucose and phosphate metabolism.

Although the theory of narcosis postulates solubility in lipoids, any drug in order to exert narcotic action must have sufficient water solubility to be carried to the central nervous system. Any prediction of the anæsthetic power of gases from the lipoid solubility curve alone would result in an erroneous conclusion. The distribution coefficient of methane between oil and water is high, but it is a relatively inefficient narcotic.

The toxicity of various anæsthetics is of different types. It may be immediate or delayed or both, manifesting itself immediately or after a lapse of time, and due to the physiologic properties of the molecule per se or due to degradation products.

The toxicity of such substances as chloroform and ethyl bromide is of a delayed type because the instability of the molecule results in the elaboration of toxic substances in vivo. Thus, although ether and chloroform may produce the same degree of anæsthesia and exist within the nervous system and the liver in respectively the same concentrations, the cells of the liver are not affected by ether but are affected by chloroform. Metabolic changes responsible for toxic symptoms such as the glycosuria of ether anæsthesia, the changes in carbon dioxide combining power, the increased

hydrogen-ion concentration of the blood, and the disturbance of phosphate distribution, so that the liver becomes richer and the muscles poorer in phosphates, are of another delayed type. Possibly rare latent disturbances following ether anæsthesia may be due to some of these conditions. The anoxemia which accompanies nitrous oxide anæsthesia does not produce such marked changes in carbon dioxide combining power of the blood as does ether anæsthesia.

Physiologic properties extraneous to that of producing anæsthesia may develop in a homologous series of substances which excludes their use as anæsthetics. Ethylene and propylene in excessive doses paralyze the respiratory center, but in the same homologous series the action of butylene is complicated by a depression of blood-pressure. The fall in blood-pressure which accompanies the use of butylene seems to be largely due to its effect on the vasomotor center. Therefore, these cells must be markedly more affected by butylene than by the other two lower members of this series, propylene and ethylene. Acetylene, with a higher degree of unsaturation than ethylene, is effective as an anæsthetic in smaller concentrations. However, the members of the triple-bonded acetylene series act differently than ethylene in its behaviour toward the ripening of fruits. Ethylene and its related compounds may function as co-enzymes for the hydrolytic enzymes of the fruit or perhaps as catalysts for hydrolytic changes. Saturation of the bond by the formation of the oxide destroys this activity. Possibly the catalytic activity is due to the addition of water with the formation of an unsaturated hydroxyl addition product which can be yielded to anhydrides.

On looking into the future one may vision much exact fundamental work yet to be done in order to substantiate or to discard controversial clinical impressions. The field of organic synthesis is open to the development of better substances for local and general anæsthesia. The question of potentiation and synergism is important and much data regarding the metabolic changes and physiologic processes that are altered during the anæsthetic state remain to be determined in order to build up knowledge from which a more complete theory of narcosis can be derived.

THE SIDNEY RAWSON WILSON PRIZE

As announced in the January number of the *British Journal of Anæsthesia* for the best INHALATION ANÆSTHESIA RESEARCH EFFORT, worthy of a premium, carried out by a citizen of the British Empire between that date and December first, 1928, a prize of Fifty Pounds is offered.

Every competitor is expected to conform to the following regulations :—

(1) To forward to the Secretary of the *British Journal of Anæsthesia* on or before the first day of December, 1928, a typewritten report of his or her work, in triplicate, with a *nom de plume* thereon, and also accompanying same a sealed envelope having the same *nom de plume* inscribed on the outside and his or her name and address within.

(2) All competitors assign to the *British Journal of Anæsthesia* all rights of publication.

(3) The *British Journal of Anæsthesia* reserves the right to decide if any effort received is of a sufficiently high grade to warrant the award.

THE ELECTROMOTIVE ACTION OF DRUGS AND A NEW THEORY OF NARCOSIS.

By R. BEUTNER.

THE new theory, presented here, tries to find a rational basis for the cause of narcosis by using as a foundation the best modern investigations on the physical nature of the process of stimulation. Independent investigations by W. Nernst and R. S. Lillie have shown that a change of electric potential differences in tissues (or a polarisation) is the underlying cause of stimulation. Narcosis, therefore, should be an inhibition of such changes. This idea can be tested by finding whether an inhibition of electromotive changes by narcotic substances occurs also outside of living tissue under various conditions. Experiments prove that this is the case, *viz.* in various artificial systems which are particularly characterized by the presence of water immiscible central conductors. In these artificial systems the addition of alcohol, ether, etc., causes the potential differences to become less variable if the concentration is changed, also less variable if toxic alkaloids are added which powerfully influence potential differences, and less variable under various other influences. An inhibition of electromotive variations is, therefore, a general property of narcotic substances. This proves that narcosis itself is essentially inhibition of polarisation as we have concluded from the work of Nernst and Lillie.

POST-ANÆSTHETIC AND POST-OPERATIVE PSYCHOSIS.

By JOHN B. DOYLE, M.D.
The Mayo Clinic, Rochester, Minnesota, Section of Neurology.

ONE of the relatively rare but distressing complications of anæsthesia and of operative surgery is psychosis. The various types of post-anæsthetic psychosis have received little consideration, since they are unusual, are generally of short duration, and have usually been described as reactions after anæsthesia. Instances of acute delirium and stupor, lasting from six to twelve hours, immediately following the induction of anæsthesia for one minute, have been described.

Two cases are reported in which patients became cyanotic in the course of anæsthesia with ethylene and oxygen and finally ceased to breathe. In both instances delirium followed recovery from the stupor, and persisted for a number of hours. Anoxemia seems the best explanation of these reactions, which are in the nature of delirium. The anoxemia may be induced by not giving oxygen, by not giving sufficient oxygen, or some gas other than oxygen, as a result of improper filling of the oxygen tank.

Twenty-eight consecutive cases of post-operative psychosis, studied at The Mayo Clinic, are reviewed and analyzed. The age incidence in the series ranged from thirty-two to sixty-nine years, with an average of forty-six. Of the twenty-eight patients, twenty were women. In the nine instances in which leukocyte counts were made the average was 16,900. The highest was 26,000 and the lowest (the only one below 10,800) was 6,700. Fever occurred in all cases, but in three

*Read before the Annual Congress of Anæsthetists, Minneapolis, Minn., June 11, 1928.

cases the temperature did not rise above 100°. In most cases, however, there was an elevation of temperature during the psychosis ranging from 100° to 103°.

In all of the cases there was an interval between the operation and the onset of the psychosis during which the patient seemed normal or relatively so. This interval varied from thirty hours to twenty-one days, with an average of a little less than five days. The average duration of the syndrome was thirteen days, with extremes of two to sixty days. In three cases death occurred during the psychosis. One patient died six days after operation, a second twenty-two days after, and a third sixty days after. Twenty-five of the twenty-eight patients recovered completely.

Sixteen of the patients had ether anæsthesia, six had ethylene, oxygen and ether, two had novocaine and ethylene, oxygen, and ether, and four had novocaine alone. The average duration of anæsthesia was forty-nine minutes; the shortest was thirteen and the longest one hundred and seven minutes. Four patients had operations on the stomach or duodenum, and five on the biliary tract; six had gynæcologic operations and five had thyroidectomy; three had operations on the large intestine and rectum, two on the urinary tract, and two had herniotomy and one had Kondoleon's operation for elephantiasis.

The psychotic manifestations were strikingly similar in most of the cases and were coloured by exaggeration of the normal tendencies of the various individuals. All of the patients showed confusion or delirium. In twenty of the twenty-eight cases the confusion was quite obvious, while the remaining eight presented evidence of delirium of varying degrees of severity.

Disturbed motility, common in this group, was unlike that seen in mania in so far as it was mild, disorganised, purposeless, and without any trend that could be followed. Flight of ideas and distractibility were not noted.

Fourteen patients had hullucinations; ten had visual hallucinations alone, one auditory hallucinations only, and three had both visual and auditory. The hallucinations were often dreamlike and of depressive character. Several patients saw

dead relatives, and one complained of seeing incense at his window.

At times the hallucinosis was marked; at others, the patients wondered whether what they appeared to see was real or imaginary. Illusions or distorted awareness were frequently described.

Delusions were present in eight instances. They were bizarre, fantastic, and continually subject to change.

None of the patients had previous psychotic episodes; but one had a familial history of mental disorder.

SUMMARY.

Post-anæsthetic psychosis is a suitable name for the type of psychic disorder that occurs occasionally at once after the induction of anoxemia during anæsthesia.

The term post-operative psychosis should be reserved for the psychiatric syndrome which appears acute several days following surgical procedures.

These forms of psychosis belong to the group of deliriums.

The prognosis is good but development of post-operative psychosis increases the mortality risk.

Treatment should be directed to dilution and elimination of toxic products, combatting starvation, and putting the patient at rest.

CYANOSIS DURING ANÆSTHESIA.

By L. F. SISE.

CYANOSIS always means anoxæmia, though the reverse is not true. Anoxæmia is frequent during anæsthesia. In fact, where the gases are used it is usually a necessary accompaniment in the production of anæsthesia.

Anoxæmia at first stimulates the respiration and circulation, but in increasing doses it depresses them and causes death, respiration usually failing before circulation. Similarly it causes first alkalosis and then acidosis. It depresses all the bodily functions and in severe degree produces structural changes.

It is an aid to the anæsthetist in producing depth of anæsthesia, and may help him in determining the plane of anæsthesia; but it is a cause of rigidity and acidosis, and is one of the most potent factors making for immediate danger to the patient.

It may well be used to advantage by the experienced and discriminating anæsthetist, but others should avoid it.

ANÆSTHESIA FOR THYROIDECTOMY.

A Study of Different Methods of Anæsthesia Used in Four Thousand Goitre Operations*.

By JOSEPH L. DECOURCY, M.D.

THE question of the method of anæsthesia is obviously of great importance in the conduct of a goitre operation. After the pre-operative use of Lugol's solution and the general improvement in operative technique during recent years, a safe anæsthetic method ranks as one of the most important factors conducive to low mortality. Pemberton[1] attributes the relative freedom from post-operative hyperthyroid crises in part to the avoidance of prolonged general anæsthesia and the use of special types of anæsthetics as well as to the general solution in modern operations.

It is true that ether and even chloroform are still frequently used for anæsthesia in goitre operations. In fact, Gwathmey[2] states that when general anæsthesia is decided upon ether and chloroform with oxygen by a tube is probably the best method of administration. With this conclusion I disagree, as my experience has been that nitrous oxide and oxygen in combination furnish by far the safest as well as an effective form of general anæsthesia.

Crile[3] has adopted the use of nitrous oxide and oxygen plus local infiltration almost as a routine in goitre surgery. By this combination he avoids the danger of psychic shock and also accomplishes anoci-association. Kocher's[4] practice was to complete the operation under local anæsthesia, and he attributed his low mortality to this method. Romanis,[5] after operating upon 250 patients with exopthalmic goitre of all types of severity—many of them with a pulse rate over 180 and some with auricular fibrillation and other gross disorganization of the heart—with a mortality of 2.4 per cent., was convinced that the death rate is much lower under local anæsthesia than under ether. Bartlett[6] believes that the ideal

* From the Surgical Section, DeCourcy Clinic.

anæsthesia for goitre operations is produced by novocaine infiltration and nitrous oxide or light ethylene inhalation.

During the past ten years approximately four thousand goitre operations were performed at the DeCourcy Clinic. From this series it is possible to make certain deductions with regard to the safety and effectiveness of different methods of anæsthesia.

The first five hundred patients were operated upon under local anæsthesia, which consisted of the free use of 0.1 per cent. cocaine. Provided the solution was injected properly, it was found that no definite limitation as to the amount used was required. Under this anæsthesia the skin incision, the cutting of the muscles and the division of the capsule were all accomplished in a satisfactory manner. But there was one drawback to the local anæsthesia: When the gland was elevated from its bed and the capsule stripped back, the patient almost invariably complained of an uncomfortable feeling; that is a sensation of being strangled. At this time he would frequently become panicky.

At that time patients who objected to local anæsthesia were given ether by the open method. This anæsthesia had the disadvantages of a stage of excitement, deep narcosis, disagreeable post-operative nausea and vomiting, and a penetrating effect on the operator and his assistants.

After completing the first five hundred cases under local anæsthesia, I began to realize that, although this technique may appear satisfactory to the operator and spectators, it is seldom appreciated by the patient. Although no pain is felt in many instances, the psychic shock is always bad, the time consumed is usually twice as long as under general anæsthesia, and the nervous tension suffered by the operator is apt to be considerable.

The second method of anæsthesia tried consisted of local infiltration combined with nitrous oxide induction and light ether sequence. For a long time this procedure was found quite satisfactory. Induction was rapid, the amount of ether used was small, the patient usually left the operating table in a conscious condition, and the stage of recovery was seldom more stormy than under local anæsthesia.

About five years ago I started to use nitrous oxide and

oxygen anæsthesia for all goitre operations. I soon found that this procedure has many advantages. The anæsthesia is not dreaded by the patient; it is induced rapidly and recovery is almost immediate. The dosage of anæsthetic can be promptly regulated to fit the individual patient and the operative field remains very quiet, thus giving the surgeon a chance to do his best work. Nerve injury can easily be detected by the change in the respiratory rate and the crowing inspiration that sets in under this light anæsthesia. There is no excess of mucus, and sufficient rigidity is maintained to keep the tongue from falling backward and thus obstructing the respiration.

If manipulations become unusually rough during the course of nitrous oxide oxygen anæsthesia, it takes but a moment to deepen the anæsthesia. Should the patient temporarily refuse to breathe, he may soon be brought back to a safe level by the administration of pure oxygen under direct pressure.

After nitrous oxide and oxygen recovery is almost immediate and the patient becomes conscious before leaving the table. Vomiting and retching are reduced to a minimum, and the danger of post-operative hæmorrhage is almost nil.

Ethylene has been tried at the Clinic but discarded. It was found to have no advantage over nitrous oxide and oxygen, and its chief objection is its unpleasant odour. Everyone connected with my surgical team complained of a persistent headache when he was present during two or more ethylene anæsthesias. Under ethylene anæsthesia bleeding from the superficial structures of the neck was aggravated in our cases. It may have been due to the excess of oxygen present in the mixture. Patients showing a tendency to vomit did not recover so promptly as from nitrous oxide and oxygen. One patient vomited incessantly for three days.

Good judgment is required in the choice of the anæsthetic. If the anæsthetist finds himself confronted with a situation wherein a given anæsthetic agent does not produce the desired result, he should without hesitation resort to other agents in order that a well-balanced anæsthesia may be produced with as little untoward result as possible prior to, during and after operation.

My belief is that every goitre operation is facilitated by nitrous oxide and oxygen anæsthesia properly administered, but the anæsthetist should be skilled in both local and general anæsthesia and prepared to give up one type and turn to another as occasion demands.

During nitrous oxide and oxygen anæsthesia the anæsthetist should attempt to keep the patient asleep and his colour natural. The skin should remain as pink as possible, whether or not the patient sleeps soundly. A vicious circle is easily established by continued cyanosis: When respiration becomes insufficient, the blood gets blue or black and the pulse weaker and weaker because of the progressive decrease of available oxygen. Lack of oxygen in turn depresses the circulation and deficient circulation diminishes oxidation. Finally a point is reached at which the circulation is insufficient to aerate the tissues even when pure oxygen is administered. When general anæsthesia is superimposed on the foundation provided by preliminary hypnotics and local anæsthetics, it should not be carried to the point at which the patient's colour changes.

About 70 per cent. of all goitre patients presenting themselves for operation do so because of urgent symptoms referred to the circulatory or respiratory apparatus. In many cases cardiac arrhythmias also are present. Practically all thyroid patients are prone to cyanosis and respiratory obstruction during some part of the operation. This condition may be due to the size or position of the gland or to the strained posture of the shoulders on the sand bag, which throws the head too far backward. In this connection obstruction in the mouth or throat must always be kept in mind.

The anæsthetist should at all times know the condition of his patient's circulation. The pulse and blood pressure ratios and reactions are pre-requisites for the interpretation of the circulatory condition. Cardiac arrhythmias affecting the rate may readily be detected in the pulse. The functional types often disappear during a carefully conducted anæsthesia; in fact, the circulation may improve with anæsthesia in functional cases. The organic types, on the other hand, either do not improve or are made worse.

By means of the sphygmomanometer *pulsus alternans*, which is an arrhythmia not necessarily affecting the rate but

characterized by alternating weak and strong heart contractions, may not only be readily detected but actually measured. Arrhythmias, particularly of this type, require close watching because they are associated with serious impairment of the muscular structure of the heart, which has lost the capacity to respond to every stimulus with a maximal contraction; in other words, the contracting capacity is diminished. In the surgery of the thyroid gland, pulsus alternans is second in frequency of the cardiac arrhythmias, and it is of particular importance because it indicates myocardial defect. Before operation the patient may exhibit no arrhythmia; but, under the stress of the manipulations, pulsus alternans occasionally develops. In such cases it is an indication that the heart muscle is unable to respond adequately to the extra effort. Pulsus alternans is encountered more frequently in hypertension, arteriosclerosis, myocarditis and nephritis. Such patients are likely to succumb promptly to a fall in blood pressure associated with an increased pulse rate.

If pulsus alternans is recognized before operation, digitalis is indicated, even though the pulse rate is not rapid. When it develops during operation, some digitalis preparation should be administered intravenously and the operation should proceed with the minimum of trauma and under the lightest possible narcosis. Morphine in sufficient dosage to produce physiologic effect is helpful, preferably administered before operation; but it may also be used with good results during the thyroidectomy.

Myocardial defects are more serious than compensated valvular disease. The crux of the matter is whether or not the circulatory mechanism is able to maintain a proper distribution of blood without cardiac exhaustion during the relatively short period of surgical intervention. A study of the individual case at the moment will show how far one may proceed with the thyroidectomy when cardiac action is impaired, but only the test of surgery will tell how the circulation will react in border-line cases of cardiac defect.

Patients with valvular defects grossly complicated with myocardial weakness require most careful anæsthesia and surgery to avoid disaster. Until the test of surgery proves the heart muscle to contain the essential reserve power to

compensate for any ordinary disturbance in blood distribution, all valvular cases must be regarded with suspicion and treated with caution.

During the ten years that I have been performing thyroidectomies I have had occasion to deal with every conceivable type of patient from the age of eleven to that of seventy. Every type of goitre has been attacked, including six malignant glands. Ligation of the superior and inferior thyroid arteries, respectively, has been employed. In some very severe cases lobectomy with removal of the remaining lobe on the following day was practiced.

In the four thousand cases at the Clinic there was but one death on the table. This accident resulted from an injury to the jugular vein, which was adherent to the thyroid capsule. One patient was anæsthetized three times in a period of two hours to permit control of hæmorrhage with no bad results. There were but two permanent cases of nerve injury.

Although the most difficult to administer, nitrous oxide and oxygen with proper preliminary medication is the anæsthetic of choice for thyroidectomy. What the patient appreciates most in this anæsthesia is the sensation of being "blown asleep." I am indebted to the dental profession for an observation which I have made with regard to the method of inducing anæsthesia with nitrous oxide. The trick is not to hold the mask against the face while inducing anæsthesia but to blow the gas into the patient's face. When this is done, the patient is free from the choking sensation so common when the mask is held firmly against the face during the induction of anæsthesia.

Nitrous oxide and oxygen anæsthesia for goitre operations would probably be a great deal more popular than it is, were it not for the fact that its administration requires considerable skill and training. It is not a method that commends itself to the lazy mind. Once mastered, however, it is most satisfactory both to the patient and the surgical team. I agree with Gwathmey, who states that "those who have never used oxygen with nitrous oxide, and who have acquired the technique of administering it alone, will be surprised by the ease and latitude given by this combination."

The best results in goitre surgery are obtained when a

surgical team of definite personnel is organized. The surgeon himself must have unbounded confidence in his first assistant, who in turn must understand and anticipate his every move. There must be a close liaison between the surgeon and the anæsthetist. The anæsthetist should be consulted frequently with regard to the advisability of doing a complete or incomplete operation in one stage, whether it would be safer to close the wound in the neck after operation or to leave it open for twenty-four to thirty-six hours.

The anæsthetist must be quick to recognize changes in the respiratory rate, the pulse rate and the colour signs, and he must understand the condition of the heart before and after operation. He must also warn the surgeon of any manipulations that are proving dangerous to the patient.

When this sort of team work is practiced as a unit for the patient's welfare, one may be assured of the highest degree of success in the surgical treatment of goitre.

Conclusions.

1. On the basis of experience in four thousand goitre operations, I believe that the combination of nitrous oxide and oxygen offers the most satisfactory form of anæsthesia for thyroidectomy.

2. The method is rather difficult and requires a trained anæsthetist. Once mastered, however, its use is highly satisfactory both to the patient and the surgical team.

3. There is no danger of asphyxia, because pure oxygen under pressure may be forced in at any time.

4. The anæsthetist should regard his patient from the point of view of an internist. He should study him carefully before, during and after operation. The use of the sphygmomanometer and the study of the blood and pulse pressures during operation are of much importance.

5. The closest possible liaison between the surgeon, his assistants and the anæsthetist is a powerful factor in reducing mortality to a minimum.

References.

1. Pemberton, J. de J. "Present-Day Surgical Treatment of Diseases of the Thyroid Gland," *J.A.M.A.*, 85: 1882, 1925.
2. Gwathmey, J. T. "Anesthesia," Ed. 2, New York, The MacMillan Co., 1925, p. 353.

3. "The Thyroid Gland," Edited by A. F. Rowland, from the Clinics of G. W. Crile and Associates, Philadelphia, W. B. Saunders Co., 1922, p. 213.
4. Kocher: Cited by Gwathmey, p. 503.
5. Romanis, W. H. C. "Surgical Treatment of Exopthalmic Goiter," *Lancet*, 1: 471, 1922.
6. Bartlett, W. "The Surgical Treatment of Goiter," St. Louis, C. V. Mosby Co., 1926, p. 152.

CONTROLLABLE SPINAL ANÆSTHESIA.

DR. GEORGE P. PITKIN, in July of last year, announced that by the employment of starch paste a viscid solution was produced which would not diffuse with the spinal fluid. Out of this has now come Spinocaine (Metz), a mixture of novocaine, strychnia and ephedrin. The viscosity is due to gliadin, the mucilaginous content of wheat starch, a method having been devised by which it was possible to extract the gliadin and render it soluble. Ephedrin has been added to stabilize the blood-pressure.

Spinocaine will not diffuse in spinal fluid but will mix with it. Thus according to Dr. Pitkin, the technique of controlling the anæsthetic and limiting its contact to only those spinal nerves that are necessary to produce anæsthesia to a definite height on the body surface, is relatively simple. It is necessary, however, to possess a working knowledge of the capacity of the dural sac, to consider the size and age of the patient, and to measure accurately the degree of Trendelenburg, to obtain the best results.

A correct amount of gliadin in the solution prevents diffusion until the anæsthetic has been absorbed by the nerve trunk. Too much gliadin greatly delays or entirely prevents anæsthesia. Too little gliadin causes the solution to be devoid of all controllable features. The viscosity of the solution causes it to remain in mass and the alcohol is sufficient to produce a specific gravity much less than the spinal fluid which makes it float in the canal as an air bubble does on a spirit level. By altering the degree of Trendelenburg the position can be regulated as desired.

Dr. Pitkin claims this method as being a great improvement over ordinary spinal anæsthesia, and the more than 9,000 successful inductions in various hospitals in America should commend it to early trials on this side of the Atlantic. Dr. Frank A. Kelly, a surgeon of Detroit, who has taken part in the development of Spinocaine, is now in England, and will give a series of demonstrations both here and on the Continent. An interesting paper by Dr. Pitkin on this subject will be published in our next number.

AVERTIN-RECTAL ANÆSTHESIA*

The Results To Date.

By Hans Killian.

IN the majority of cases injury to the human organs has not been ascertained. Benthin found, now and again, urobilin and urobilinogen in the urine. Reisckauer mentions a case of fatty degeneration of the liver (including heart and kidneys). The kidneys are frequently injured. Berchardt mentions hæmorrhagic nephritis (quoted from Unger), red blood plates and hyaline tubules in the urine. Nordmann, Kirschner and Melzner report the same. One case of Melzner showed, at the post-mortem examination, epithelial destruction in the kidney. The nephritis generally disappeared within six days.

Abdomen and Intestines.

Avertin per os often caused singultus. (This was separately discovered by Eckstein and Romminger). There exists a possibility of the creation of decomposition-products in the intestine itself. (Darmflora). The frequency of intestinal disturbances has surely been considerably lessened, perhaps set aside, by the new Eicholtz procedure of preparing the solution.

Clinical proofs are not yet available. The decomposition-products cause inflammation of the mucous membranes of the intestines, discharge of hæmorrhagic mucus with severe tenesmus, and other intestinal conditions.

Enteritis generally disappears in two to six days without further consequences. Children are especially endangered in cases of dyspeptic disturbances. But rectal etheroil-narcosis is said also to cause considerable disturbances to the intestines.

* Continued from April Number. Reprinted from *Narkose und Anæsthesie*, January 1928, by kind permission of the Editor. The translation is ours.

SURGERY.

The large clinics have observed caution in its use and some are even adverse (compare also Schwalbe). Nordmann, Unger, Haas, Butzengeiger, Lohenhoffe, Vogler, Schrödel, Kreuter and others have come forward for rectal-narcosis, though with reservations. As avertin has been given for examinations (there are now said to be over a hundred a day), the reports have in part turned out very incomplete and have not at all come up to the modern requirements of careful testing. Furthermore, the majority cannot make comparisons with gas-narcosis (the apparatus still being far too expensive, rectal-narcosis requiring no apparatus).

As a sleep-producer and sedative, avertin has been successfully used in tetanus by Laewen, Haas, and, as per information received by letter, has been praised and used by Kirschner. In the five patients reported on considerable relief was experienced, the cramp disappearing, they could sleep, and it was possible to administer nourishment during the intervals. Repetitions (20 narcoses in thirteen days, often three times daily, Laewen) did no harm. Two patients died. Effect upon the course of the disease is not to hand.

The exact *spheres* of *indication,* if one may now speak in that manner, are disputed. However, it is generally agreed that it is contra-indicated in patients suffering from dysentery, hæmorrhoids, fistula, etc., and in individuals with low blood-pressure. The majority of observers exclude heart and kidney patients, and especially those having liver complications, also the moribund, cachectic, and anæmic, as well as small children. Compensated heart cases are considered more favourably. Because of the greater danger of shock its use in laparotomy will probably have to be limited because the tension of the abdominal walls only disappears with large doses. Apart from this, the prospect of strain during the stage of excitement causing too great tension upon the sutures, impels caution. One is not at all clear about its usefulness in urologic surgery. The proximity of the rectum must be considered. The use in minor surgery does not come into question because of the prolonged after-effect. Lobenhoffer excludes avertin in urgent operations. E. makes it a rule to exclude avertin on principle after hæmorrhage, during or after traumatic shock, (*i.e.*, in

the field), and in cases debilitated by long-standing discharges.

Avertin-rectal-narcosis seems to be indicated especially where a mask cannot easily be applied, (*i.e.*, in operations at the head and neck). It is especially recommended by Sauerbruch, Schrödel and Nordmann, recently also by Schmiedem, for Basedow's disease operation because of its quietening effect. That is comprehensible. But even in such cases there have been total failures and a serious stage of excitement. Few operations on the skull have been carried out as they frequently run a critical course. For these avertin would only be considered in exceptional cases. Butzengeiger suggests rectal-narcosis for endoscopic (bladder?) operations of all kinds. If the remedy were totally harmless one could eventually agree to this, but bladder-reflexes only disappear under the deepest narcosis, necessitating great doses.

Gynæcology and Obstetrics.

Opinions are still more divided in the sphere of gynæcology than in that of general surgery. Some have tried to use avertin for twilight-sleep (Conrad, Benthin, Martin).

Technical difficulties arise. When the head was in the centre of the pelvis or at the bottom of it, the course was difficult and imperfect. The waters were often pressed out with the first pains. Labour-remedies acted promptly in spite of avertin. The heart of the child remains uninfluenced. All children were born in good condition. While Martin tried to manage with 0.06 pro kg., Benthin always used in cases of labour 0.1. *Post partum* atony is to be feared. Greater pauses and a weakening of the travail has been observed. Obstetrical forceps were difficult. The narcosis does not last out for perineal stitches. The times of labour were remarkably short. Rectal narcosis in labour must be used cautiously where there is a question of sepsis.

The uncertainty in the choice of the right moment for beginning the rectal-narcosis was annoying. For manual manipulations avertin is contra-indicated. As against this Polano advises rectal-narcosis for clinical enquiry and instruction purposes..

As regards gynæcological operations the same rules apply as in general surgery. 0.1 was not sufficient, a minimum of

0.125 or 0.15 was necessary. Benthin reports a case of placenta previa with avertin. Whether in gynæcological heart-cases avertin would be suitable is a question. The use of it in eclampsia has only been carried through and favourably judged by Benthin.

In children avertin has often failed. Eckstein, Romminger and Trendtel rightly bring to the fore the exceeding sensitiveness of the important vital centres of a child, especially during illness. For hæmorrhagic surgical operations on a child higher doses were necessary, therefore the danger is increased. Asphyxias, collapses etc. were observed. Two cases of death are known (Hedonal seems to have done better). Contra-indication exists in the case of seriously ill children, and dyspeptics. In heart cases, premature children and those suffering from whooping cough, asphyxia may be expected.

Epilogue.

Avertin is in the first place a useful sleep-producer and sedative. If one desires to go beyond this and attain full-narcosis, then one demands of the molecule more than it is able to perform without injuring the human organism. The ever present harmful effect on the circulatory apparatus with narcotic doses causes a heightened shock-readiness, a state in which the human organism is not always able to bear another shock such as that caused by operation-trauma, especially in the case of laparotomy..

Thus may be explained the occasional catastrophy. To introduce into the organism a molecule with properties so decidedly injurious to the vital centres in a single dose without knowledge of individual rapidity of absorption is dangerous, and the molecule is less to blame for it than the actual procedure of the narcosis. For more than 30 years rectal narcosis has been tried again and again, and has always been given up, because in opposition to inhalation-narcosis it is not possible either to decide on the precise dose nor to interrupt the narcosis when once produced.

That the process of divided doses lessens the danger, I consider probable, that it fully sets it aside, I consider improbable. Furthermore, the recent blood-pressure-tests of E. contradict the principle of divided doses. The majority of

the complications occurred in the first 30 minutes. The fact that the absorbing surface of the intestinal mucous membrane always varies, that it is unknown beforehand, and that the osmotic faculty is also unknown, throws a dark shadow on the whole method.

An anæsthetic must guarantee the greatest possible measure of safety. In this respect, avertin-rectal-narcosis cannot in the least compare with other anæsthetics. So one can only agree conscienciously with the use of E. 107 as a sleep producer, and a sedative, but must observe the greatest care when using it as an anæsthetic because too high doses are necessary for this purpose.

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4. Glass aquariums with openings on two sides to carry rubber stoppers through which glass tubes were inserted for the incoming and outgoing gases. These were placed on glass slabs to which they were adapted. The experiments on guinea pigs and rabbits were made usually with these containers.

At the Dusseldorf Krankenhaus, Dr. Franken adapted an ordinary rubber surgical glove for the experiments we made there with acetylene-oxygen upon a dog. The wrist portion was adapted over the nose and mouth. One of the fingers is slipped over an inlet tube. One of the other rubber fingers was so cut that it flapped open only when the supply of gases was excessive.

The gas machines used were the Metric Model Gwathmey apparatus, and a four feed Gwathmey model to which water manometers were attached. The calibrations were checked with a gas meter and a stop-watch. The Metric Model is well known. The other model some of you have seen me demonstrate at the British Medical Association Conference in Nottingham in 1926.

THE STABILITY OF ANÆSTHETIC ETHER.*

By F. W. Nitardy and N. W. Tapley.

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THAT traces of peroxides will form in anæsthetic ether during storage has been a matter of common knowledge for many years. From time to time statements have appeared in the scientific press discussing methods of measuring the quantity of peroxides present and suggesting means for their removal, as well as means for treating ether to prevent their formation. None of the latter recommendations, however, have proved of value in eliminating or even controlling their development. Of recent years, the Pharmacopœias of the world have included tests for peroxides while the medical press has published results of investigations indicating that respiratory and nervous complications observed in certain cases after ether anæsthesia occurred simultaneously with the presence of peroxides in the ether. Unfortunately, relatively little had been accomplished until recently with the study of ether peroxides, due, in part, to their highly explosive nature and the consequent difficulty of isolating them. While it is manifestly difficult to demonstrate by clinical experiment or physiological test that the trace of peroxides often present in ordinary anæsthetic ether is responsible for the adverse reactions reported, the evidence, nevertheless, is such as to make freedom from peroxides a highly desirable condition in anæsthetic ether.

While much research work has been done during recent years, the problem of understanding the causes and nature of reactions involved in peroxide formation has not been solved, in fact it has proven unusually baffling. Intensive

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work, however, has disclosed that peroxides form in pure ether more readily than was formerly believed, *i.e.*, the formation of peroxides can be demonstrated in practically 100 per cent. of all containers of anæsthetic ether if sufficiently frequent examinations are made. Furthermore, the peroxides which have developed will disappear again in time, so that very old ether is usually peroxide free. During the disappearance of the peroxides, aldehydes often appear, but these too ultimately vanish, leaving as an end-product of the entire reaction, a trace of an organic acid. This formation of foreign substances and their subsequent disappearance is rather erratic as far as the time element is concerned. It may be said, however, that most anæsthetic ether will form peroxides within six months after manufacture and that in all probability they will remain in the ether for a year or more before disappearing. It is not unusual to find containers of ether from the same lot varying widely in this respect, the container undoubtedly having considerable influence as well as the conditions of storage, and the degree of freedom from mechanical impurities, such as dust, soldering flux and similar contaminants. In general, impure or contaminated ether will take a longer time to develop peroxides than a clean ether of high quality. Exposure to light and heat also stimulates peroxide formation, while storage in the dark and in the cold retards it. Any ether of sufficient purity to be suitable for anæsthetic purposes will, however, definitely develop peroxides when stored in any of the ordinary containers which, in the past, have been in commercial use, namely, in tin cans or glass bottles.

Through an exhaustive study of the influence of the container on the stability of ether, the Squibb Laboratories discovered that the formation of peroxides in ether can be prevented. The work leading to this discovery was an investigation of catalysts and anticatalysts in the reaction causing the development of peroxide. Preliminary experiments indicated that copper, copper alloys and even tarnished, oxidized, and "green" copper when placed in bottles or cans of ether would act as an anticatalyst. All of the bottles containing copper remained peroxide-free, while all of the controls showed the presence of peroxides as indicated by the U.S.P. test.

These encouraging results were confirmed by more carefully controlled experiments which included a determination of the relation of the area of copper to the protective action it afforded, and proved that considerable area was needed for complete protection. Under controlled storage conditions prevailing in this work, ether in glass bottles or tin cans usually showed the presence of peroxides in from one to eight months, with the majority of containers giving a positive test at the end of a four months' period. The same ether, when exposed to heat and pressure in such containers would show the presence of peroxides in one hour. With an adequate surface of copper exposed in the container, no peroxides or aldehydes developed under storage conditions now extending for over two and a half years and, under heat and pressure treatment, extending for 60 hours.

It was further shown that peroxides cannot be removed by placing ether containing peroxides in a copper container, thus demonstrating definitely that copper prevents their formation rather than removing them after they are formed. Complete chemical and physical examination at monthly intervals on hundreds of cans of ether stored in copper plated and other containers has shown the former to be the only container in which ether may be stored and remain unchanged in every particular over prolonged periods and under temperature variations such as one must expect to encounter under ordinary conditions of commerce.

In conclusion, we can make the following generalizations:

1. Peroxides do not exist in freshly prepared, pure anæsthetic ether but develop as a result of changes in materials originally pure.

2. Any ether of sufficient purity to be suitable for anæsthetic purposes will develop peroxides in time when stored in any of the ordinary containers, which in the past have been in commercial use, such as tin cans or glass bottles.

3. The formation of peroxides can be prevented by packaging ether in containers, the interior of which presents an adequate surface of copper.

4. Contact with an adequate surface of copper preserves anæsthetic ether in its original pure condition.

5. Copper does not remove peroxides from deteriorated ether.

Our studies are being continued in the hope that we will ultimately understand the reactions which underlie peroxide formation, why they eventually disappear, as well as why they do not form when ether is stored in contact with copper. For the present, however, there is a good deal of satisfaction to be derived from the knowledge that the marketing of ether in copper or copper plated containers at least eliminates, so far as is known to-day, the difficulty that has been universally encountered by ether manufacturers in this country as well as abroad, and that this discovery insures to the anæsthetist the opportunity to obtain anæsthetic ether which he may be reasonably sure to be peroxide free regardless of how long or short a time it may have been kept in stock or under what conditions of temperature, etc., it may have been stored.

In order to demonstrate the effect of copper, there is on exhibition samples of the same ether stored in glass with and without the presence of copper, in ordinary tin containers, and in tin containers the interior of which is copper plated. Tests will be applied to demonstrate that this ether has developed peroxides, both by storage in glass and in the usual tin containers, but when stored in contact with copper, no peroxides were developed, even though the storage and all other conditions were identical. We have also a few cans which have been cut open so as to show the copper coating on the interior of the cans.

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CONCLUSIONS FROM EXTENDED EXPERIMENTS WITH NITROUS OXIDE, ACETYLENE, ETHYLENE OXYGEN ANÆSTHESIAS[1]

JULIUS D. GOLDMAN, B.S., D.D.S.

1. Gas[2]-oxygen is a safe anæsthetic.

2. Anæsthesia can be maintained for long periods and return to consciousness ensues in from 15 seconds to 3 minutes. Some albino rats and white mice anæsthetised from 3 to 7 hours, when placed into the open air were on their feet and walking in about 15 to 30 seconds. On the average, after these long anæsthesias, the animals commenced walking about in less than a minute. Cats arose to their feet usually in a minute and commenced walking about in less than another 30 seconds.

3. A number of white mice and albino rats I anæsthetised every other day for two months for periods averaging one hour (10 minutes to 7 hours). There was no noticeable after effects. In these cases nitrous oxide, or ethylene, or acetylene was administered with oxygen: and combinations of these gases with oxygen.

4. At times a small quantity of anæsthol was mixed with these gases. With the same animal, when anæsthol was added toward the conclusion of the anæsthesia, the period of return to consciousness was always lengthened. In longer anæsthesias when anæsthol was added during the early part of the induction or maintenance, followed by gas-oxygen alone for 15 minutes or more, return to consciousness came almost as speedily as when no anæsthol was given.

1. Read before the New York Society of Anæsthetists, April 5th, 1928.

2. In this report I use the word " gas " to mean nitrous oxide, or ethylene or acetylene; or a combination of any two of these gases; or a mixture of the three gases.

5. Thus far I have not been able to secure an apparatus sufficiently accurate to measure the strength of the anæsthol in the gas-oxygen mixture.

6. With acetylene-oxygen or with a combination of acetylene-nitrous oxide oxygen, or acetylene-ethylene oxygen, an even plane of anæsthesia is secured speedily (1 to 5 minutes) and maintained easily.

7. With nitrous-oxide-oxygen I found it more difficult to secure and maintain an even plane of anæsthesia than with either of the hydro-carbon gases and oxygen. When anæsthol or ether was added to the nitrous-oxide-oxygen I found it easier to secure and maintain an even plane of anæsthesia.

8. With nitrous oxide, anæsthesia was not secured unless the oxygen supply was less than 7 per cent.

9. With ethylene, anæsthesia was not secured unless the oxygen supply was below 12 per cent.

10. With acetylene, anæsthesia was generally secured with an oxygen supply of 20 to 30 per cent. With rabbits and guinea pigs the oxygen supply was frequently reduced as low as 8 per cent. for from 1 to 3 minutes before anæsthesia was secured.

11. With nitrous oxide, anæsthesia could not be maintained for more than 3 minutes intervals if the oxygen supply was above 12 per cent.

12. With ethylene, anæsthesia could not be maintained for more than 3 minute intervals if the oxygen supply was above 15 per cent.

13. With acetylene, anæsthesia was maintained for hours with the oxygen at 30 per cent.

14. With acetylene, anæsthesia was maintained for hours with the oxygen at 40 per cent.

15. With acetylene, anæsthesia was maintained for hours with the oxygen at 50 per cent.

16. Wiht acetylene, anæsthesia secured at 20 per cent., oxygen for 2 minutes, the oxygen increased to 30 per cent., anæsthesia remained at an even plane ½ to one hour, the oxygen increased at 40 per cent., in another ½ hour the oxygen raised to 50 per cent., and then to 60 per cent. At times the animals then showed signs of waking and the oxygen was

reduced to 20 per cent. or 30 per cent. for 1 to 2 minutes, followed by an increase of oxygen to 55 per cent. when the anæsthesia remained even for ½ hour or more.

17. With acetylene, the animals were frequently troubled by salivation. At times I discontinued the anæsthesia when the saliva obstructed the breathing passages markedly. Frequently I removed the animal from the anæsthesia chamber, wiped away the saliva, and the animal still asleep was returned to the chamber and the anæsthesia continued. With ethylene-oxygen, or nitrous-oxide-oxygen, or nitrous-oxide-ethylene-oxygen salivation was not a disturbing factor.

18. With nitrous-oxide-oxygen, cyanosis is almost always present.

19. With ethylene-oxygen cyanosis is not so marked, but slight cyanosis is generally present.

20. With acetylene-oxygen, anæsthesia can be maintained with no cyanosis.

21. With nitrous-oxide-oxygen, if ether is added, anæsthesia can be maintained with little or no cyanosis.

22. With nitrous-oxide-acetylene oxygen, anæsthesia can be maintained with no cyanosis.

23. With nitrous-acetylene-oxygen, anæsthesia can be maintained with no cyanosis.

24. In nitrous-oxide-oxygen anæsthesia the oxygen varies from 4 to 8 per cent. In the majority of cases if an increase of more than 1 per cent. oxygen is administered signs of waking will appear in about one minute. At no time was I able to increase the oxygen 5 per cent. above the 5 per cent. or more oxygen that was being given without symptoms of light anæsthesia, or loss of anæsthesia appearing in ½ to two minutes. For instance, when I administered 6 per cent. oxygen waking generally occurred in one minute if I increased that to 8 per cent. If I increased the oxygen from 5 to 10 per cent. or from 6 to 11 per cent. waking always occurred in from 20 seconds to 2 minutes.

25. Disturbance in breathing or difficult breathing I always considered a danger sign. In every case when the animal was immediately upon the appearance of this symptom placed into the open air, it got to its feet in from 10 seconds

to 3 minutes and commenced walking about in another 10 to 30 seconds.

26. With acetylene-oxygen and with nitrous-oxide-acetylene oxygen when disturbance in breathing or difficult breathing occurred I was able to continue the anæsthesia and secure regular breathing by altering the percentage of gases administered; or in some cases by wiping away the saliva which might have been the cause of the disturbance.

27. With gas-oxygen whenever upon stoppage of breathing the animal was at once placed in the open air it got to its feet in 15 seconds to 5 minutes. In some cases with acetylene-oxygen or acetylene-nitrous-oxide-oxygen; or with ethylene-oxygen; or with nitrous-oxide-ethylene-oxygen when stoppage of breathing occurred I did not remove the animal to the open, but increased the oxygen and breathing returned. In other instances I did not change the mixture of gases and breathing returned. In some instances of stoppage of breathing I removed the animal from the gas chamber, inserted a small rubber tube into the mouth of the animal and insufflated the animal with my expiration, and breathing returned in a few seconds.

Apparatus.

The chambers in which the animals were placed were:—

1. Glass bottles of various sizes into which white mice and albino rats could be placed with ease. Rubber stoppers were adapted to these, into which a gas inlet and an exit tube were inserted, of a quarter inch caliber glass. Rubber tubing connected the inlet tube with the gas machine. Between the glass inlet tube and the rubber tubing a small rubber bag was sometimes placed.

2. As the above, except that the bottoms of the bottles were cut off, so that by merely lifting the bottles off a glass base the animals could easily be examined at any time during the anæsthesia.

3. For cats a wooden box was constructed, with a glass sliding door through which the animals were inserted or removed. Two sides of the box carried one opening each for the insertion of a rubber stopper carrying a glass tube each, for the ingress and egress of the gases.

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